comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

27. (Amended) A method for enhancing immune cell infiltration into a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

REMARKS

Reconsideration of the instant application in view of the above amendments and the following remarks is respectfully requested. Claims 1-33 are pending. Claims 2, 17 and 27 have been amended to more specifically define the claimed subject matter. Support for these amendments may be found, for example, at page 10, lines 23-31. No new matter has been added.

As an initial matter, Applicants thank the Examiner for acknowledging the allowability of claims 1, 6, 26 and 31.

Rejection under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 2-5, 7-15, 17-18, 20-25, 27-30, and 32-33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that does not have sufficient written description. More specifically, the Action asserts that the present specification does not sufficiently describe a modulating agent comprising an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that does not contain a LYHY motif.

To facilitate allowance and without acquiescing to the assertions in the Action, Applicants have amended claims 2, 17 and 27 to specify that the recited occludin cell adhesion recognition sequence comprises the LYHY motif. Applicants respectfully submit that the present application has provided sufficient support for the currently claimed subject matter. For instance, the present application describes occludin cell adhesion recognition sequences that

comprise the LYHY motif (*see*, *e.g.*, page 10, lines 15-31), In addition, the present application also describes various antibodies raised against occludin cell adhesion recognition sequences (*see*, *e.g.*, page 30, line 1, to page 31, line 15). It is noted that the Patent Office regards an antibody against an antigen that is well characterized by a specification as sufficiently supported if at the time of filing, the production of antibodies was conventional (*see*, *e.g.*, Example 16 of Synopsis of Application of Written Description Guidelines). In the instance case, because at the time of the present invention, the production of antibodies against a well characterized antigen was conventional, Applicants believe that the present application provides sufficient written description for the claimed invention.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. § 112, first paragraph, has been overcome. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 16-25 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled. More specifically, the Action notes that these claims do not recite the administration of a cell adhesion modulating agent with another drug having an anti-tumor activity. The Action asserts that there is no guidance in the specification that would clearly indicate that a peptide with the motif LYHY or a cell adhesion modulating agent was solely responsible for cancer treatment. The Action further asserts that the present specification, with regard to the use of cell adhesion modulating agents for treating cancer, is confined to broad allegations and suggestions without substantiating working examples.

Applicants respectfully traverse this ground of rejection. With respect to enablement, nothing more than objective enablement is required in order to meet the requirements of 35 U.S.C. § 112, first paragraph. In particular, as stated by the Board of Patent Appeals and Interferences:

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Staehelin v. Secher, 24 USPQ 2d 1513, 1516 (B.P.A.I. 1992) (citing *In re*

Marzocchi 169 USPQ 367, 369 (C.C.P.A. 1971)) (emphasis original).

In the instant case, a rational basis that the present specification fails to enable the claimed subject matter has not been established in the Office Action. No specific support is provided for doubting that one of ordinary skill in the art, in view of the teachings in the present application, would be able to use cell adhesion modulating agents in treating cancer without undue experimentation. Should this ground of rejection be maintained, Applicants respectfully request that specific support be provided.

Additionally, Applicants respectfully submit that the present application provides sufficient disclosure to enable the claimed methods of using cell adhesion modulating agents in treating cancer. For instance, the section entitled "Cell Adhesion Modulating Agents" (*see, e.g.*, page 10, line 1 to page 31, line 15) contains a detailed description on how to make cell adhesion modulating agents. The section entitled "Evaluation of Modulating Agent Activity" (*see, e.g.*, page 31, line 17 to page 36, line 8) discloses various assays that may be used to evaluate the activity of a candidate cell adhesion modulating agent. The section entitled "Modulating Agent Modification and Formulations" (*see, e.g.*, page 36, line 11 to page 41, line 9) teaches how to modify or formulate modulating agents. In addition, the present application describes the use of cell adhesion modulating agents alone in inhibiting angiogenesis (*see, e.g.*, page 47, line 10 to page 48, line 17) or in treating cancer (*see, e.g.*, page 45, line 1 to page 46, line 9).

Furthermore, it is noted that the mere fact that exemplified embodiments in the specification are more limited than those recited in the claims does not provide sufficient reason for a non-enablement rejection. An applicant is *not* required to specifically exemplify all embodiments of the invention that are encompassed by the invention. The enablement requirement can be fulfilled by the use of *illustrative* examples *or* broad terminology. *In re* Anderson, 176 USPQ 331 (CCPA 1973).

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. § 112, first paragraph, has been overcome. Withdrawal of this rejection is respectfully requested.

Information Disclosure Statement

In the Office Action the Examiner states that the Jaeger *et al.* reference has not been considered since the incorrect reference was provided. Enclosed is a copy of the Jaeger reference, along with a copy of a related reference not previously cited. Applicants also enclose

a Supplemental Information Disclosure Statement, a PTO-1449 showing these references, and the required fee of $180.

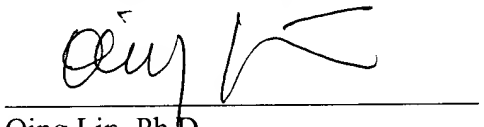
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made**."

On the basis of the above amendments and remarks, reconsideration of the application and its allowance are respectfully requested. Should the Examiner have any additional questions, he is respectfully encouraged to contact the undersigned attorney at (206) 622-4900.

Respectfully submitted,

Orest Blaschuk et al.

SEED Intellectual Property Law Group PLLC



Qing Lin, Ph.D.
(See Limited Recognition in File)

QXL:jab

Enclosures:
Supplemental IDS, PTO-1449 and Cited References (2)

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 2, 17 and 27 have been amended as follows:

2. (Amended) A method for enhancing the delivery of a drug to a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

17. (Amended) A method for treating cancer in a mammal, comprising administering to a mammal a cell adhesion modulating agent, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

27. (Amended) A method for enhancing immune cell infiltration into a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises an antibody or fragment thereof that specifically binds to an occludin cell adhesion recognition sequence that comprises the sequence LYHY (SEQ ID NO:1), and wherein said modulating agent inhibits occludin-mediated cell adhesion.

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